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09/747,287	12/22/2000	Beverly Packard	300-948600US	9292

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EXAMINER
KAM, CHIH MIN

ART UNIT	PAPER NUMBER
1653	6

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/747,287	Applicant(s) PACKARD ET AL.
	Examiner Chih-Min Kam	Art Unit 1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-102 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-102 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 90-102 are cited as dependent from claim 85, it appears they are dependent from claim 89. To advance prosecution, claims 90-102 are treated as dependent from claim 89.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U. S. C. 121:

I. Claims 1-12 and 24-31, drawn to a fluorogenic composition comprising a polypeptide backbone joining two fluorophores of the same species, where the fluorophores form an H-dimer resulting in the quenching of the fluorescence, classified in class 514, subclass 2.

II. Claims 1 and 13-31, drawn to a fluorogenic composition comprising a nucleic acid backbone joining two fluorophores of the same species, where the fluorophores form an H-dimer resulting in the quenching of the fluorescence, classified in class 536, subclass 23.1.

III. Claims 32-46, drawn to a mammalian cell comprising fluorogenic composition comprising a polypeptide backbone or a nucleic acid backbone joining two identical fluorophores, where the fluorophores form an H-dimer resulting in quenching of the fluorescence, classified in class 435, subclass 325.

IV. Claims 48-65, drawn to a method of detecting the activity of a protease using the fluorogenic composition comprising a polypeptide backbone joining two fluorophores of the same species, where the fluorophores form an H-dimer resulting in the quenching of the fluorescence, classified in class 514, subclass 2, and class 435, subclass 219.

V. Claims 66-83, drawn to a method of detecting the activity of a nuclease or the presence of a nucleic acid using the fluorogenic composition comprising a nucleic acid backbone joining two fluorophores of the same species, where the fluorophores form an H-dimer resulting in the quenching of the fluorescence, classified in 536, subclass 23.1, and 435, subclass 199.

VI. Claims 84-88, drawn to a method of detecting the interaction of a first and a second molecule, the method comprising providing a first molecule having a first fluorophore, providing a second molecule having a second fluorophore, wherein the first fluorophore and the second fluorophore are the same species, when juxtaposed, form an H-dimer resulting in the quenching of the fluorescence, classified in class 536, subclass 23.1, and 514, subclass 2.

VII. Claims 89-102, drawn to a method of detecting a change in conformation or cleavage of a macromolecule using the macromolecule having attached two fluorophores of the same species, where the fluorophores form an H-dimer resulting in the quenching of the fluorescence, classified in class 514, subclass 2, and class 536, subclasses 23.1, and 1.11.

Should Invention III be elected, applicant is required to select either polypeptide backbone or nucleic acid backbone from claim 32 because the polypeptide and the nucleic acid are physically and functionally distinct chemical entities and have different utilities. This is not species election.

Should Invention VI be elected, applicant is required to select a receptor and a receptor ligand, an antibody and antigen, a lectin and a carbohydrate, or a nucleic acid and a nucleic acid

binding protein from claim 85 as the first molecule and the second molecule because the receptor, the antibody, the lectin and the nucleic acid are physically and functionally distinct chemical entities and have different utilities. This is not species election.

Should Invention VII be elected, applicant is required to select a polypeptide, a nucleic acid, a lipid, a polysaccharide or an oligosaccharide from claim 90 as the macromolecule because they are physically and functionally distinct chemical entities and have different utilities. This is not species election.

3. The inventions are distinct, each from the other because of the following reasons:

Inventions I, II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to a polypeptide, a nucleic acid and a mammalian cell, which are patentably distinct each from the other because they are physically and functionally distinct chemical entities and have different utilities.

The product of Invention I and the methods of Inventions IV and VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the methods of Inventions IV and VII are alternative processes of use of the product of Invention I.

The product of Invention I is distinct from the methods of Inventions V and VI because the product of Invention I can be neither made by nor used in the methods of Inventions V and VI.

The product of Invention II and the methods of Inventions V and VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the methods of Inventions V and VII are alternative processes of use of the product of Invention II.

The product of Invention II is distinct from the methods of Inventions IV and VI because the product of Invention II can be neither made by nor used in the methods of Inventions IV and VI.

The product of Invention III is distinct from the methods of Inventions IV-VII because the product of Invention III can be neither made by nor used in the methods of Inventions IV-VII.

The methods of Inventions IV-VII are distinct from each other because the method steps and outcomes are wholly different among Inventions IV-VII.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and recognized divergent subject matter, and because inventions I-VII require different searches but are not co-extensive, examination of these distinct inventions would pose a serious burden on the examiner and therefore restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement is traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

A telephone call was made to Tom Hunter on April 4, 2003 to request an oral election to the above restriction requirement, but did not result in an election being made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

Christopher S. F. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

April 4, 2003

CLAIMS

WHAT IS CLAIMED IS:

1. A fluorogenic composition comprising a polypeptide backbone or a nucleic acid backbone joining two fluorophores of the same species whereby said fluorophores form an H-dimer resulting in quenching of the fluorescence of said fluorophores.

2. The fluorogenic composition of claim 1, wherein said composition comprises a polypeptide backbone.

3. The fluorogenic composition of claim 2, wherein said polypeptide backbone comprises a protease binding site ranging in length from about 2 to about 15 amino acids.

4. The fluorogenic composition of claim 2, wherein said polypeptide backbone comprises a protease binding site ranging in length from about 2 to about 8 amino acids.

5. The fluorogenic composition of claim 2, wherein said polypeptide backbone ranges in length from about 4 to about 31 amino acids.

6. The fluorogenic composition of claim 2, wherein said composition is attached to a solid support.

7. The fluorogenic composition of claim 2, wherein said composition is inside a mammalian cell.

8. The fluorogenic composition of claim 2, wherein said composition bears a hydrophobic group.

9. The fluorogenic composition of claim 8, wherein said hydrophobic group is selected from the group consisting of: Fmoc, 9-fluoreneacetyl group, 1-fluorenecarboxylic group, 9-florenecarboxylic group, and 9-fluorenone-1-carboxylic group, benzyloxycarbonyl, Xanthyl (Xan), Trityl (Trt), 4-methyltrityl (Mtt), 4-methoxytrityl (Mmt), 4-methoxy-2,3,6-trimethyl-benzenesulphonyl (Mtr), Mesitylene-2-sulphonyl (Mts), 4,4'-dimethoxybenzhydryl (Mbh),Tosyl (Tos), 2,2,5,7,8-pentamethyl chroman-6-sulphonyl

(Pmc), 4-methylbenzyl (MeBzl), 4-methoxybenzyl (MeOBzl), Benzyloxy (BzlO), Benzyl (Bzl), Benzoyl (Bz), 3-nitro-2-pyridinesulphenyl (Npys), 1-(4,4-dimentyl-2,6-diaxocyclohexylidene)ethyl (Dde), 2,6-dichlorobenzyl (2,6-DiCl-Bzl), 2-chlorobenzyloxycarbonyl (2-Cl-Z), 2-bromobenzyloxycarbonyl (2-Br-Z), Benzyloxymethyl (Bom), t-butoxycarbonyl (Boc), cyclohexyloxy (cHxO),t-butoxymethyl (Bum), t-butoxy (tBuO), t-Butyl (tBu), Acetyl (Ac), and Trifluoroacetyl (TFA).

10. The composition of claim 9, wherein said hydrophobic group is Fmoc.

11. The composition of claim 9, wherein said hydrophobic group is Fa.

12. The composition of claim 9, wherein said hydrophobic group is attached to the amino terminus of the molecule.

13. The fluorogenic composition of claim 1, wherein said composition comprises a nucleic acid backbone.

14. The fluorogenic composition of claim 13, wherein said nucleic acid backbone comprises a restriction site.

15. The fluorogenic composition of claim 13, wherein said nucleic acid backbone is self-complementary and forms a hairpin.

16. The fluorogenic composition of claim 13, wherein said nucleic acid backbone ranges in length from about 10 to about 100 nucleotides.

17. The fluorogenic composition of claim 13, wherein said nucleic acid backbone ranges in length from about 15 to about 50 nucleotides.

18. The fluorogenic composition of claim 13, wherein said composition is attached to a solid support.

19. The fluorogenic composition of claim 13, wherein said composition is inside a mammalian cell.

20. The fluorogenic composition of claim 13, wherein said composition bears a hydrophobic group.

21. The fluorogenic composition of claim 20, wherein said hydrophobic group is selected from the group consisting of Fmoc, 9-fluoreneacetyl group, 1-fluorenecarboxylic group, 9-florenecarboxylic group, and 9-fluorenone-1-carboxylic group, benzyloxycarbonyl, Xanthyl (Xan), Trityl (Trt), 4-methyltrityl (Mtt), 4-methoxytrityl (Mmt), 4-methoxy-2,3,6-trimethyl-benzenesulphonyl (Mtr), Mesitylene-2-sulphonyl (Mts), 4,4'-dimethoxybenzhydryl (Mbh),Tosyl (Tos), 2,2,5,7,8-pentamethyl chroman-6-sulphonyl (Pmc), 4-methylbenzyl (MeBzl), 4-methoxybenzyl (MeOBzl), Benzyloxy (BzlO), Benzyl (Bzl), Benzoyl (Bz), 3-nitro-2-pyridinesulphenyl (Npys), 1-(4,4-dimentyl-2,6-diaxocyclohexylidene)ethyl (Dde), 2,6-dichlorobenzyl (2,6-DiCl-Bzl), 2-chlorobenzyloxycarbonyl (2-Cl-Z), 2-bromobenzyloxycarbonyl (2-Br-Z), Benzyloxymethyl (Bom), t-butoxycarbonyl (Boc), cyclohexyloxy (cHxO),t-butoxymethyl (Bum), t-butoxy (tBuO), t-Butyl (tBu), Acetyl (Ac), and Trifluoroacetyl (TFA).

22. The composition of claim 21, wherein said hydrophobic group is Fmoc.

23. The composition of claim 21, wherein said hydrophobic group is Fa.

24. The fluorogenic composition of claim 1, wherein said fluorophores are linked to the nucleic acid backbone or to the polypeptide backbone by linkers.

25. The fluorogenic composition of claim 1, wherein said fluorophores have an excitation wavelength between about 310 nm and about 750 nm.

26. The fluorogenic composition of claim 1, wherein said fluorophores are selected from the group consisting of carboxytetramethylrhodamine, carboxyrhodamine-X, carboxyrhodamine 110, diethylaminocoumarin, and carbocyanine dyes.

27. The fluorogenic composition of claim 1, wherein said fluorophores are carboxytetramethylrhodamine.

28. The fluorogenic composition of claim 1, wherein said fluorophores are carboxyrhodamine-X.

29. The fluorogenic composition of claim 1, wherein said fluorophores are carboxyrhodamine 110.

30. The fluorogenic composition of claim 1, wherein said fluorophores are diethylaminocoumarin.

31. The fluorogenic composition of claim 1, wherein said fluorophores are carbocyanine dyes.

32. A mammalian cell comprising a fluorogenic composition comprising a polypeptide backbone or a nucleic acid backbone joining two identical fluorophores whereby said fluorophores form an H-dimer resulting in the quenching of the fluorescence of said fluorophores.

33. The cell of claim 32, wherein said composition comprises a polypeptide backbone.

34. The cell of claim 32, wherein said composition comprises a nucleic acid backbone.

35. The cell of claim 32, wherein said composition bears a hydrophobic group.

36. The cell of claim 35, wherein said hydrophobic group is selected from the group consisting of: Fmoc, 9-fluoreneacetyl group, 1-fluorenecarboxylic group, 9-florenecarboxylic group, and 9-fluorenone-1-carboxylic group, benzyloxycarbonyl, Xanthyl (Xan), Trityl (Trt), 4-methyltrityl (Mtt), 4-methoxytrityl (Mmt), 4-methoxy-2,3,6-trimethyl-benzenesulphonyl (Mtr), Mesitylene-2-sulphonyl (Mts), 4,4'-dimethoxybenzhydryl (Mbh),Tosyl (Tos), 2,2,5,7,8-pentamethyl chroman-6-sulphonyl (Pmc), 4-methylbenzyl (MeBzl), 4-methoxybenzyl (MeOBzl), Benzyloxy (BzlO), Benzyl (Bzl), Benzoyl (Bz), 3-nitro-2-pyridinesulphenyl (Npys), 1-(4,4-dimentyl-2,6-diaxocyclohexylidene)ethyl (Dde), 2,6-dichlorobenzyl (2,6-DiCl-Bzl), 2-chlorobenzyloxycarbonyl (2-Cl-Z), 2-bromobenzyloxycarbonyl (2-Br-Z), Benzyloxymethyl (Bom), t-butoxycarbonyl (Boc), cyclohexyloxy (cHxO),t-butoxymethyl (Bum), t-butoxy (tBuO), t-Butyl (tBu), Acetyl (Ac), and Trifluoroacetyl (TFA).

37. The cell of claim 36, wherein said hydrophobic group is Fmoc.

38. The cell of claim 32, wherein said hydrophobic group is Fa.

39. The cell of claim 32, wherein said hydrophobic group is attached to the amino terminus of the molecule.

40. The cell of claim 32, wherein said fluorophores are linked to the nucleic acid backbone or to the polypeptide backbone by linkers.

41. The cell of claim 32, wherein said fluorophores have an excitation wavelength between about 310 nm and about 750 nm.

42. The cell of claim 32, wherein said fluorophores are selected from the group consisting of carboxytetramethylrhodamine, carboxyrhodamine-X, carboxyrhodamine 110, diethylaminocoumarin, and carbocyanine dyes.

43. The cell of claim 42, wherein said fluorophores are carboxytetramethylrhodamine.

44. The cell of claim 42, wherein said fluorophores are carboxyrhodamine-X.

45. The cell of claim 42, wherein said fluorophores are carboxyrhodamine 110.

46. The cell of claim 42, wherein said fluorophores are diethylaminocoumarin.

47. The cell of claim 42, wherein said fluorophores are carbocyanine dyes.

48. A method of detecting the activity of a protease, said method comprising:

i) contacting said protease with a fluorogenic composition comprising a polypeptide backbone joining two fluorophores of the same species whereby said fluorophores form an H-dimer resulting in quenching of the fluorescence of said fluorophores; and

ii) detecting a change in fluorescence or absorbance of said fluorogenic composition where an increase in fluorescence or a change in absorbance indicates that said protease cleaves said polypeptide backbone.

49. The method of claim 48, wherein said polypeptide backbone comprises a protease binding site ranging in length from about 2 to about 15 amino acids.

50. The method of claim 48, wherein said polypeptide backbone comprises a protease binding site ranging in length from about 2 to about 8 amino acids.

51. The method of claim 48, wherein said composition is attached to a solid support.

52. The method of claim 48, wherein said composition is inside a mammalian cell.

53. The method of claim 48, wherein said composition is inside a insect cell.

54. The method of claim 48, wherein said composition is inside a yeast cell.

55. The method of claim 48, wherein said composition bears a hydrophobic group.

56. The method of claim 48, wherein said hydrophobic group is selected from the group consisting of: Fmoc, 9-fluoreneacetyl group, 1-fluorenecarboxylic group, 9-florenecarboxylic group, and 9-fluorenone-1-carboxylic group, benzyloxycarbonyl, Xanthyl (Xan), Trityl (Trt), 4-methyltrityl (Mtt), 4-methoxytrityl (Mmt), 4-methoxy-2,3,6-trimethyl-benzenesulphonyl (Mtr), Mesitylene-2-sulphonyl (Mts), 4,4'-dimethoxybenzhydryl (Mbh),Tosyl (Tos), 2,2,5,7,8-pentamethyl chroman-6-sulphonyl (Pmc), 4-methylbenzyl (MeBzl), 4-methoxybenzyl (MeOBzl), Benzyloxy (BzlO), Benzyl (Bzl), Benzoyl (Bz), 3-nitro-2-pyridinesulphenyl (Npys), 1-(4,4-dimentyl-2,6-diaxocyclohexylidene)ethyl (Dde), 2,6-dichlorobenzyl (2,6-DiCl-Bzl), 2-chlorobenzyloxycarbonyl (2-Cl-Z), 2-bromobenzyloxycarbonyl (2-Br-Z), Benzyloxymethyl (Bom), t-butoxycarbonyl (Boc), cyclohexyloxy (cHxO),t-butoxymethyl (Bum), t-butoxy (tBuO), t-Butyl (tBu), Acetyl (Ac), and Trifluoroacetyl (TFA).

57. The method of claim 56, wherein said hydrophobic group is attached to the amino terminus of the molecule.

58. The method of claim 48, wherein said fluorophores are linked to the nucleic acid backbone or to the polypeptide backbone by linkers.

59. The method of claim 48, wherein said fluorophores have an excitation wavelength between about 310 nm and about 750 nm.

60. The method of claim 48, wherein said fluorophores are selected from the group consisting of carboxytetramethylrhodamine, carboxyrhodamine-X, carboxyrhodamine 110, diethylaminocoumarin, and carbocyanine dyes.

61. The method of claim 48, wherein said contacting is in a histological section.

62. The method of claim 48, wherein said contacting is in a cell culture.

63. The method of claim 48, wherein said contacting is contacting a seeded or cultured adherent cell.

64. The method of claim 48, wherein said contacting is in a cell suspension derived from a biological sample selected from the group consisting of a tissue, blood, urine, saliva, lymph, biopsy.

65. The method of claim 48, wherein said detecting is by a method selected from the group consisting of fluorescence microscopy, confocal microscopy, fluorescence microplate reader, flow cytometry, fluorometry, and absorption spectroscopy.

66. A method of detecting the activity of a nuclease or the presence of a nucleic acid, said method comprising:

i) contacting said nuclease or said nucleic acid with a fluorogenic composition comprising a nucleic acid backbone joining two fluorophores of the same species whereby said fluorophores form an H-dimer resulting in quenching of the fluorescence of said fluorophores; and

ii) detecting a change in fluorescence or absorbance of said fluorogenic composition where an increase in fluorescence or a change in absorbance indicates that said nuclease cleaves said nucleic acid backbone or that said nucleic acid hybridizes to said backbone.

67. The method of claim 66, wherein said nucleic acid backbone comprises a restriction site.

68. The method of claim 66, wherein said nucleic acid backbone is self-complementary and forms a hairpin.

69. The method of claim 66, wherein said nucleic acid backbone ranges in length from about 10 to about 100 nucleotides.

70. The method of claim 66, wherein said nucleic acid backbone ranges in length from about 15 to about 50 nucleotides.

71. The method of claim 66, wherein said composition is attached to a solid support.

72. The method of claim 66, wherein said composition is inside a mammalian cell.

73. The method of claim 66, wherein said composition is in solution.

74. The method of claim 66, wherein said composition bears a hydrophobic group.

75. The method of claim 74, wherein said hydrophobic group is selected from the group consisting of: Fmoc, 9-fluoreneacetyl group, 1-fluorenecarboxylic group, 9-florenecarboxylic group, and 9-fluorenone-1-carboxylic group, benzyloxycarbonyl, Xanthyl (Xan), Trityl (Trt), 4-methyltrityl (Mtt), 4-methoxytrityl (Mmt), 4-methoxy-2,3,6-trimethyl-benzenesulphonyl (Mtr), Mesitylene-2-sulphonyl (Mts), 4,4'-dimethoxybenzhydryl (Mbh),Tosyl (Tos), 2,2,5,7,8-pentamethyl chroman-6-sulphonyl (Pmc), 4-methylbenzyl (MeBzl), 4-methoxybenzyl (MeOBzl), Benzyloxy (BzlO), Benzyl (Bzl), Benzoyl (Bz), 3-nitro-2-pyridinesulphenyl (Npys), 1-(4,4-dimentyl-2,6-diaxocyclohexylidene)ethyl (Dde), 2,6-dichlorobenzyl (2,6-DiCl-Bzl), 2-chlorobenzyloxycarbonyl (2-Cl-Z), 2-bromobenzyloxycarbonyl (2-Br-Z), Benzyloxymethyl (Bom), t-butoxycarbonyl (Boc), cyclohexyloxy (cHxO),t-butoxymethyl (Bum), t-butoxy (tBuO), t-Butyl (tBu), Acetyl (Ac), and Trifluoroacetyl (TFA).

76. The method of claim 66, wherein said fluorophores are linked to the nucleic acid backbone or to the polypeptide backbone by linkers.

77. The method of claim 66, wherein said fluorophores have an excitation wavelength between about 310 nm and about 750 nm.

78. The method of claim 66, wherein said fluorophores are selected from the group consisting of carboxytetramethylrhodamine, carboxyrhodamine-X, carboxyrhodamine 110, diethylaminocoumarin, and carbocyanine dyes.

79. The method of claim 66, wherein said contacting is in a histological section.

80. The method of claim 66, wherein said contacting is in a cell culture.

81. The method of claim 66, wherein said contacting is contacting a seeded or cultured adherent cell.

82. The method of claim 66, wherein said contacting is in a cell suspension derived from a biological sample selected from the group consisting of a tissue, blood, urine, saliva, lymph, biopsy.

83. The method of claim 66, wherein said detecting is by a method selected from the group consisting of fluorescence microscopy, confocal microscopy, fluorescence microplate reader, flow cytometry, fluorometry, and absorption spectroscopy.

84. A method of detecting the interaction of a first and a second molecule, said method comprising:

i) providing a first molecule having a first fluorophore attached thereto;

ii) providing a second molecule having a second fluorophore attached thereto wherein said first fluorophore and said second fluorophore are the same species of fluorophore and, when juxtaposed, form an H-dimer thereby quenching fluorescence produced by the fluorophores; and

iii) detecting a change in fluorescence or absorbance produced by said fluorophores where a decrease in fluorescence or a change in absorbance indicates that the first molecule and the second molecule are interacting.

85. The method of claim 84, wherein said first molecule and said second molecule are selected from the group consisting of a receptor and a receptor ligand, an antibody and an antigen, a lectin and a carbohydrate, and a nucleic acid and a nucleic acid binding protein.

86. The method of claim 84, wherein said fluorophore is linked to said first molecule by a linker.

87. The method of claim 84, wherein said fluorophores have an excitation wavelength between about 310 nm and about 750 nm.

88. The method of claim 84, wherein said fluorophores are selected from the group consisting of carboxytetramethylrhodamine, carboxyrhodamine-X, carboxyrhodamine 110, diethylaminocoumarin, and carbocyanine dyes.

89. A method of detecting a change in conformation or cleavage of a macromolecule, said method comprising:

i) providing a macromolecule having attached thereto two fluorophores of the same species whereby said fluorophores form an H-dimer resulting in quenching of the fluorescence of said fluorophores; and

ii) detecting a change in fluorescence or absorbance of said fluorophores wherein a change in fluorescence or absorbance indicates a change in conformation or cleavage of said macromolecule.

90. The method of claim 89, wherein said macromolecule is selected from the group consisting of a polypeptide, a nucleic acid, a lipid, a polysaccharide, and an oligosaccharide.

91. The method of claim 89, wherein said macromolecule is attached to a solid support.

92. The method of claim 89, wherein said macromolecule is inside a mammalian cell.

93. The method of claim 89, wherein said macromolecule bears a hydrophobic group.

94. The method of claim 93, wherein said hydrophobic group is selected from the group consisting of: Fmoc, 9-fluoreneacetyl group, 1-fluorenecarboxylic group, 9-florenecarboxylic group, and 9-fluorenone-1-carboxylic group, benzyloxycarbonyl, Xanthyl (Xan), Trityl (Trt), 4-methyltrityl (Mtt), 4-methoxytrityl (Mmt), 4-methoxy-2,3,6-trimethyl-benzenesulphonyl (Mtr), Mesitylene-2-sulphonyl (Mts), 4,4'-dimethoxybenzhydryl (Mbh),Tosyl (Tos), 2,2,5,7,8-pentamethyl chroman-6-sulphonyl (Pmc), 4-methylbenzyl (MeBzl), 4-methoxybenzyl (MeOBzl), Benzyloxy (BzlO), Benzyl (Bzl), Benzoyl (Bz), 3-nitro-2-pyridinesulphenyl (Npys), 1-(4,4-dimentyl-2,6-diaxocyclohexylidene)ethyl (Dde), 2,6-dichlorobenzyl (2,6-DiCl-Bzl), 2-chlorobenzyloxycarbonyl (2-Cl-Z), 2-bromobenzyloxycarbonyl (2-Br-Z), Benzyloxymethyl (Bom), t-butoxycarbonyl (Boc), cyclohexyloxy (cHxO),t-butoxymethyl (Bum), t-butoxy (tBuO), t-Butyl (tBu), Acetyl (Ac), and Trifluoroacetyl (TFA).

95. The method of claim 85, , wherein said fluorophores are linked to the macromolecule by linkers.

96. The method of claim 85, wherein said fluorophores have an excitation wavelength between about 310 nm and about 750 nm.

97. The method of claim 85, wherein said fluorophores are selected from the group consisting of carboxytetramethylrhodamine, carboxyrhodamine-X, carboxyrhodamine 110, diethylaminocoumarin, and carbocyanine dyes.

98. The method of claim 85, wherein said contacting is in a histological section.

99. The method of claim 85, wherein said contacting is in a cell culture.

100. The method of claim 85,, wherein said contacting is contacting a seeded or cultured adherent cell.

101. The method of claim 85,, wherein said contacting is in a cell suspension derived from a biological sample selected from the group consisting of a tissue, blood, urine, saliva, lymph, biopsy.

102. The method of claim 85, wherein said detecting is by a method selected from the group consisting of fluorescence microscopy, fluorescence microplate reader, flow cytometry, fluorometry, confocal microscopy, and absorption spectroscopy.